

## Accepted Manuscript

Overcoming Multiple Gastrointestinal Barriers by Bilayer Modified Hollow Mesoporous Silica Nanocarriers

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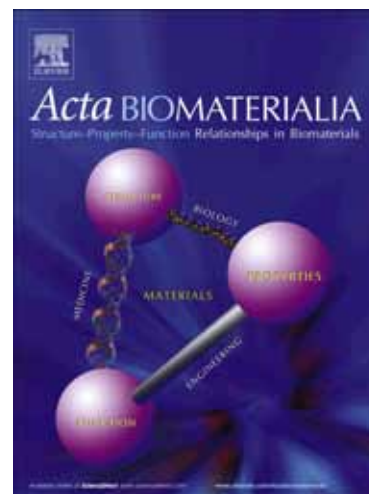
PII: S1742-7061(17)30654-2  
DOI: <https://doi.org/10.1016/j.actbio.2017.10.025>  
Reference: ACTBIO 5131

To appear in: *Acta Biomaterialia*

Received Date: 3 July 2017  
Revised Date: 10 October 2017  
Accepted Date: 13 October 2017

Please cite this article as: Wang, Y., Zhao, Y., Cui, Y., Zhao, Q., Zhang, Q., Musetti, S., Kinghorn, K.A., Wang, S., Overcoming Multiple Gastrointestinal Barriers by Bilayer Modified Hollow Mesoporous Silica Nanocarriers, *Acta Biomaterialia* (2017), doi: <https://doi.org/10.1016/j.actbio.2017.10.025>

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**Overcoming Multiple Gastrointestinal Barriers by Bilayer Modified Hollow  
Mesoporous Silica Nanocarriers**

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**Abstract**

Oral administration of nanocarriers remains a significant challenge in the pharmaceutical sciences. The nanocarriers must efficiently overcome multiple gastrointestinal barriers including the harsh gastrointestinal environment, the mucosal layer, and the epithelium. Neutral hydrophilic surfaces are reportedly necessary for mucus permeation, but hydrophobic and cationic surfaces are important for efficient epithelial absorption. To accommodate these conflicting surface property requirements, we developed a strategy to modify nanocarrier surfaces with cationic cell-penetrating peptides (CPP) concealed by a hydrophilic succinylated casein (SCN) layer. SCN is a mucus-inert natural material specifically degraded in the intestine, thus protecting nanocarriers from the harsh gastric environment, facilitating their mucus permeation, and inducing exposure of CPPs after degradation for further

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